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NEWS	3	Jun 03	New e-mail delivery for search results now available
NEWS	4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	7	Sep 03	JAPIO has been reloaded and enhanced
NEWS	8	Sep 16	Experimental properties added to the REGISTRY file
NEWS	9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	11	Oct 24	BEILSTEIN adds new search fields
NEWS	12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	13	Nov 18	DKILIT has been renamed APOLLIT
NEWS	14	Nov 25	More calculated properties added to REGISTRY
NEWS	15	Dec 04	CSA files on STN
NEWS	16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	17	Dec 17	TOXCENTER enhanced with additional content
NEWS	18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS	20	Feb 13	CANCERLIT is no longer being updated
NEWS	21	Feb 24	METADEX enhancements
NEWS	22	Feb 24	PCTGEN now available on STN
NEWS	23	Feb 24	TEMA now available on STN
NEWS	24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	25	Feb 26	PCTFULL now contains images
NEWS	26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	27	Mar 20	EVENTLINE will be removed from STN
NEWS	28	Mar 24	PATDPAFULL now available on STN
NEWS	29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS	30	Apr 11	Display formats in DGENE enhanced
NEWS	31	Apr 14	MEDLINE Reload
NEWS	32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS	34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	35	Apr 28	RDISCLOSURE now available on STN
NEWS	36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS	38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS	39	May 16	CHEMREACT will be removed from STN
NEWS	40	May 19	Simultaneous left and right truncation added to WSCA
NEWS	41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS	42	Jun 06	Simultaneous left and right truncation added to CBNB

NEWS 43 Jun 06 PASCAL enhanced with additional data

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> file medline, biosis, wpids, dgene, embase, jicst, fsta
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=> s DNA binding protein
L1   38218 DNA BINDING PROTEIN

=> s zinc finger
L2   35192 ZINC FINGER

=> s l1 and method
L3   5412 L1 AND METHOD

=> s cys2-his2 class
L4   66 CYS2-HIS2 CLASS

=> s l4 and l2
L5   64 L4 AND L2

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=> s l5 and nucleic acid binding protein
   4 FILES SEARCHED...
L6             0 L5 AND NUCLEIC ACID BINDING PROTEIN

=> s l5 and l1
L7             3 L5 AND L1

=> d l7 ti abs ibib tot

L7   ANSWER 1 OF 3  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI   ZINC FINGER-DNA RECOGNITION ANALYSIS OF BASE
     SPECIFICITY BY SITE-DIRECTED MUTAGENESIS.
AB   Zinc fingers of the Cys2/His2 class are
     conserved 28 - 30 amino acid motifs that constitute an important and
     widespread family of eukaryotic DNA-binding domains. It is therefore of
     great interest to understand the rules that govern specific recognition of
     DNA by zinc fingers. The DNA-binding domain of the transcription factor
     Krox-20 consists of three zinc fingers, each of them making its primary
     contacts with a three-base pair subsite. We have performed a data
     base-guided site-directed  mutagenesis analysis of Krox-20: nine
     derivatives were generated, in which one to three amino acid changes has
     been introduced within finger 2, at positions which were likely to affect
     the specificity of DNA recognition. The affinities of the different
     proteins for a panel of potential DNA binding sites were estimated by gel
     retardation assay. Six of the derivatives bound specific targets with
     affinities comparable to that of wild type Krox-20 for its consensus
     binding site. However, the specificity of recognition was dramatically
     modified at the expected bases, in a manner that could be explained by
     examining the newly introduced amino acids within the context of the
     overall finger/triplet interaction. These data provide new insights into
     the details of zinc finger-DNA interactions and,
     combined with the modular nature of zinc fingers, illustrate both the
     potential and the difficulties of utilizing these motifs for designing
     DNA-binding proteins with novel specificities.
ACCESSION NUMBER:    1992:501357  BIOSIS
DOCUMENT NUMBER:     BA94:119882
TITLE:               ZINC FINGER-DNA RECOGNITION ANALYSIS OF
                     BASE SPECIFICITY BY SITE-DIRECTED MUTAGENESIS.
AUTHOR(S):           NARDELLI J; GIBSON T; CHARNAY P
CORPORATE SOURCE:    LAB. GENETIQUE MOL., CNRS D 1302, ECOLE NORMALE SUPERIEURE,
                     46 RUE D'ULM, F-75230 PARIS CEDEX 05, FR.
SOURCE:              NUCLEIC ACIDS RES, (1992) 20 (16), 4137-4144.
                     CODEN: NARHAD. ISSN: 0305-1048.
FILE SEGMENT:        BA; OLD
LANGUAGE:            English

L7   ANSWER 2 OF 3  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI   MOLECULAR CLONING SEQUENCING AND MAPPING OF EGR2 A HUMAN EARLY GROWTH
     RESPONSE GENE ENCODING A PROTEIN WITH ZINC-BINDING FINGER STRUCTURE.
AB   Early growth response gene-1 (Egr-1) is a mouse gene displaying fos-like
     induction kinetics in diverse cell types following mitogenic stimulation.
     Egr-1 encodes a protein with "zinc-binding finger" structure. Zinc fingers
     are a protein structural motif that serve as DNA-binding domains in
     several transcriptional regulatory proteins. Using low-stringency
     hybridization with an Egr-1 cDNA probe, we identified a distinct human
     cDNA (designated EGR2 for early growth response gene-2), which is
     coregulated with EGR1 by fibroblast and lymphocyte mitogens; however,
     several stimuli that induce Egr-1 mRNA in PC12 (rat pheochromocytoma)
     cells do not induce Egr-2mRNA. The cDNA sequence predicts a protein of 406
     amino acids, including three tandem zinc fingers of the Cys2-
     His2 class. Strikingly, the deduced amino acid sequences
     of human EGR2 and mouse Egr-1 are 92% identical in the zinc
     finger region but show no similarity elsewhere. EGR2 maps to human
     chromosome 10 at bands q21-22. Structure-function analysis of EGR2 and
```

EGR1 proteins should provide insight into the mechanisms linking signal transduction and transcriptional regulation of gene expression.

ACCESSION NUMBER: 1989:4810 BIOSIS
DOCUMENT NUMBER: BA87:4810
TITLE: MOLECULAR CLONING SEQUENCING AND MAPPING OF EGR2 A HUMAN EARLY GROWTH RESPONSE GENE ENCODING A PROTEIN WITH ZINC-BINDING FINGER STRUCTURE.
AUTHOR(S): JOSEPH L J; LE BEAU M M; JAMIESON G A JR; ACHARYA S; SHOWS T B; ROWLEY J D; SUKHATME V P
CORPORATE SOURCE: DEP. MED., HOWARD HUGHES MED. INST., UNIV. CHICAGO, CHICAGO, ILL. 60637.
SOURCE: PROC NATL ACAD SCI U S A, (1988) 85 (19), 7164-7168. CODEN: PNASA6. ISSN: 0027-8424.
FILE SEGMENT: BA; OLD
LANGUAGE: English

L7 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI The zebrafish egr1 gene encodes a highly conserved, **zinc-finger** transcriptional regulator.
AB The Egr family of transcriptional regulators comprises a group of genes that encode members of the **Cys2-His2 class** of **zinc finger** proteins. We have isolated a zebrafish egr1 homolog by screening a zebrafish genomic library with a mouse Egr1 **zinc finger** probe. Southern blotting indicated the existence of single zebrafish egr1 gene and, as in higher vertebrates, the presence of related members of a larger gene family. Sequence analysis of the zebrafish egr1 coding region revealed a high level of homology to the mouse, rat, and human egr1 genes with the notable exception of a polymorphic, triplet nucleotide repeat sequence in the region coding for the amino terminus of the Egr1 protein. The predicted DNA-binding, **zinc finger** domain protein sequence was strictly conserved. The 5' region of the zebrafish egr1 gene contained a variety of transcription factor binding sites, also present in the mouse gene, for serum response factor, CREB, and c-ets. The zebrafish egr1 transcript was approximately 3.4 kb in size and was expressed in adult zebrafish brain and muscle RNA, a pattern of expression similar to that observed in mice. The potential for zebrafish egr1 to function as a transcriptional regulator was tested by constructing an expression vector containing zebrafish egr1 coding sequences under the control of a cytomegalovirus promoter. This construct was found to activate transcription of a reporter plasmid bearing multiple Egr1 binding sites when transiently cotransfected into mouse 3T3 cells. Our results indicate that the structure, regulation, and function of the Egr1 gene have been highly conserved during vertebrate evolution and suggest an important role for this gene in growth and development.

ACCESSION NUMBER: 94377814 EMBASE
DOCUMENT NUMBER: 1994377814
TITLE: The zebrafish egr1 gene encodes a highly conserved, **zinc-finger** transcriptional regulator.
AUTHOR: Drummond I.A.; Rohwer-Nutter P.; Sukhatme V.P.
CORPORATE SOURCE: Renal Division, Department of Medicine, Harvard Med. Sch./Beth Israel Hosp., 330 Brookline Avenue,Boston, MA 02215, United States
SOURCE: DNA and Cell Biology, (1994) 13/9 (953-961). ISSN: 1044-5498 CODEN: DCEBE8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

=> d his

(FILE 'HOME' ENTERED AT 18:27:32 ON 10 JUN 2003)

FILE 'MEDLINE, BIOSIS, WPIDS, DGENE, EMBASE, JICST-EPLUS, FSTA' ENTERED
AT 18:27:49 ON 10 JUN 2003
L1 38218 S DNA BINDING PROTEIN
L2 35192 S ZINC FINGER
L3 5412 S L1 AND METHOD
L4 66 S CYS2-HIS2 CLASS
L5 64 S L4 AND L2
L6 0 S L5 AND NUCLEIC ACID BINDING PROTEIN
L7 3 S L5 AND L1

=> d l5 ti abs ibib 1-10

L5 ANSWER 1 OF 64 MEDLINE
TI Retrovirally expressed metal response element-binding transcription factor-1 normalizes metallothionein-1 gene expression and protects cells against zinc, but not cadmium, toxicity.
AB Metal response element (MRE) transcription factor-1 (MTF1), a member of the **Cys2-His2 class** of **zinc-finger** transcription factors, is best known for its robust transcriptional regulation of mammalian metallothionein (MT) genes. MTF1 is also believed to play a generalized role in regulating genes involved in protection against heavy metals and oxidative stress. MTF1 binding to MRE motifs is regulated by changes in intracellular zinc (Zn(2+)) concentration. Molecular dissection of MTF1 has been hindered by its high constitutive trans-activity following transient transfection and the failure of these systems to examine genes packaged in native chromatin. In developing a system to avoid these problems, we employed a high-efficiency retroviral transduction system to reintroduce MTF1 into mouse Mtf1(-/-) knockout cells (dko7). Electrophoretic mobility shift assays demonstrated that MTF1 retrovirally transduced dko7 cells (MTF1dko7) possess levels of inducible MTF1-MRE binding activity similar to that seen in mouse hepatoma Hepa-1 cells, and MTF1 binding could be modulated over a 20-fold range by varying the concentration of Zn(2+) present in the culture medium. The dko7 cells exhibited no change in Mt1 gene expression upon Zn(2+) or cadmium (Cd(2+)) treatment; in contrast, in MTF1dko7 cells, Zn(2+) or Cd(2+) induced MT1 mRNA accumulation in a dose-dependent manner. Interestingly, MTF1dko7 cells showed resistance to Zn(2+) toxicity, but negligible resistance to Cd(2+). Concomitantly, MT1 protein levels in MTF1dko7 cells were inducible to the same degree as that in Hepa-1 cells when treated with Zn(2+), but not with Cd(2+). Together, our studies suggest that MTF1-mediated regulation of gene expression is sufficient to protect cells against Zn(2+) toxicity and may be necessary but not sufficient to protect cells against Cd(2+) toxicity.
2002 Elsevier Science (USA).
ACCESSION NUMBER: 2002120545 MEDLINE
DOCUMENT NUMBER: 21674936 PubMed ID: 11814329
TITLE: Retrovirally expressed metal response element-binding transcription factor-1 normalizes metallothionein-1 gene expression and protects cells against zinc, but not cadmium, toxicity.
AUTHOR: Solis Willy A; Childs Nicole L; Weedon Michael N; He Lei; Nebert Daniel W; Dalton Timothy P
CORPORATE SOURCE: Center for Environmental Genetics, University of Cincinnati Medical Center, Cincinnati, Ohio 45267-0056, USA.
CONTRACT NUMBER: P30 ES06096 (NIEHS)
R01 AG09235 (NIA)
R01 ES10416 (NIEHS)
SOURCE: TOXICOLOGY AND APPLIED PHARMACOLOGY, (2002 Jan 15) 178 (2) 93-101.
Journal code: 0416575. ISSN: 0041-008X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020222
Last Updated on STN: 20020308
Entered Medline: 20020307

L5 ANSWER 2 OF 64 MEDLINE
TI High-resolution structures of variant Zif268-DNA complexes: implications for understanding **zinc finger**-DNA recognition.
AB BACKGROUND: Zinc fingers of the **Cys2-His2 class** comprise one of the largest families of eukaryotic DNA-binding motifs and recognize a diverse set of DNA sequences. These proteins have a relatively simple modular structure and key base contacts are typically made by a few residues from each finger. These features make the **zinc finger** motif an attractive system for designing novel DNA-binding proteins and for exploring fundamental principles of protein-DNA recognition. RESULTS: Here we report the X-ray crystal structures of **zinc finger**-DNA complexes involving three variants of Zif268, with multiple changes in the recognition helix of finger one. We describe the structure of each of these three-finger peptides bound to its corresponding target site. To help elucidate the differential basis for site-specific recognition, the structures of four other complexes containing various combinations of these peptides with alternative binding sites have also been determined. CONCLUSIONS: The protein-DNA contacts observed in these complexes reveal the basis for the specificity demonstrated by these Zif268 variants. Many, but not all, of the contacts can be rationalized in terms of a recognition code, but the predictive value of such a code is limited. The structures illustrate how modest changes in the docking arrangement accommodate the new sidechain-base and sidechain-phosphate interactions. Such adaptations help explain the versatility of naturally occurring **zinc finger** proteins and their utility in design.
ACCESSION NUMBER: 1998230744 MEDLINE
DOCUMENT NUMBER: 98230744 PubMed ID: 9562555
TITLE: High-resolution structures of variant Zif268-DNA complexes: implications for understanding **zinc finger**-DNA recognition.
AUTHOR: Elrod-Erickson M; Benson T E; Pabo C O
CORPORATE SOURCE: Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.
CONTRACT NUMBER: 5T32GM08334 (NIGMS)
SOURCE: STRUCTURE, (1998 Apr 15) 6 (4) 451-64.
Journal code: 9418985. ISSN: 0969-2126.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980619

L5 ANSWER 3 OF 64 MEDLINE
TI Zif268 protein-DNA complex refined at 1.6 A: a model system for understanding **zinc finger**-DNA interactions.
AB BACKGROUND: Zinc fingers of the **Cys2 His2 class** recognize a wide variety of different DNA sequences and are one of the most abundant DNA-binding motifs found in eukaryotes. The previously determined 2.1 A structure of a complex containing the three zinc fingers from Zif268 has served as a basis for many modeling and design studies, and Zif268 has proved to be a very useful model system for studying how TFIIIA-like zinc fingers recognize DNA. RESULTS: We have refined the structure of the Zif268 protein-DNA complex at 1.6 A

resolution. Our structure confirms all the basic features of the previous model and allows us to focus on some critical details at the protein-DNA interface. In particular, our refined structure helps explain the roles of several acidic residues located in the recognition helices and shows that the zinc fingers make a number of water-mediated contacts with bases and phosphates. Modeling studies suggest that the distinctive DNA conformation observed in the Zif268-DNA complex is correlated with finger-finger interactions and the length of the linkers between adjacent fingers. Circular dichroism studies indicate that at least some of the features of this distinctive DNA conformation are induced upon complex formation. CONCLUSIONS: Our 1.6 A structure should provide an excellent framework for analyzing the effects of Zif268 mutations, for modeling related **zinc finger**-DNA complexes, and for designing and selecting Zif268 variants that will recognize other DNA sites.

ACCESSION NUMBER: 97094974 MEDLINE
DOCUMENT NUMBER: 97094974 PubMed ID: 8939742
TITLE: Zif268 protein-DNA complex refined at 1.6 A: a model system for understanding **zinc finger**-DNA interactions.
AUTHOR: Elrod-Erickson M; Rould M A; Nekludova L; Pabo C O
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.
SOURCE: STRUCTURE, (1996 Oct 15) 4 (10) 1171-80. Journal code: 9418985. ISSN: 0969-2126.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970128

L5 ANSWER 4 OF 64 MEDLINE

TI The zebrafish egr1 gene encodes a highly conserved, **zinc-finger** transcriptional regulator.

AB The Egr family of transcriptional regulators comprises a group of genes which encode members of the **Cys2-His2 class** of **zinc-finger** proteins. We have isolated a zebrafish egr1 homologue by screening a zebrafish genomic library with a mouse Egr1 **zinc finger** probe. Southern blotting indicated the existence of a single zebrafish egr1 gene and, as in higher vertebrates, the presence of related members of a larger gene family. Sequence analysis of the zebrafish egr1 coding region revealed a high level of homology to the mouse, rat, and human Egr1 genes with the notable exception of a polymorphic, triplet nucleotide repeat sequence in the region coding for the amino terminus of the Egr1 protein. The predicted DNA-binding, **zinc-finger** domain protein sequence was strictly conserved. The 5' region of the zebrafish egr1 gene contained a variety of transcription factor binding sites, also present in the mouse gene, for serum response factor, CREB and c-Ets. The zebrafish egr1 transcript was approximately 3.4 kb in size and was expressed in adult zebrafish brain and muscle RNA, a pattern of expression similar to that observed in mice. The potential for zebrafish egr1 to function as a transcriptional regulator was tested by constructing an expression vector containing zebrafish egr1 coding sequences under the control of a cytomegalovirus promoter. This construct was found to activate transcription of a reporter plasmid bearing multiple Egr1 binding sites when transiently cotransfected into mouse 3T3 cells. Our results indicate that the structure, regulation, and function of the Egr1 gene have been highly conserved during vertebrate evolution and suggest an important role for this gene in growth and development.

ACCESSION NUMBER: 95032735 MEDLINE

DOCUMENT NUMBER: 95032735 PubMed ID: 7945937
TITLE: The zebrafish egr1 gene encodes a highly conserved, **zinc-finger** transcriptional regulator.
AUTHOR: Drummond I A; Rohwer-Nutter P; Sukhatme V P
CORPORATE SOURCE: Harvard Medical School, Boston, MA.
CONTRACT NUMBER: CA40046 (NCI)
SOURCE: DNA AND CELL BIOLOGY, (1994 Oct) 13 (10) 1047-55.
Journal code: 9004522. ISSN: 1044-5498.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U12895
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941209

L5 ANSWER 5 OF 64 MEDLINE
TI The zebrafish egr1 gene encodes a highly conserved, **zinc-finger** transcriptional regulator.
AB The Egr family of transcriptional regulators comprises a group of genes that encode members of the **Cys2-His2 class** of **zinc finger** proteins. We have isolated a zebrafish egr1 homolog by screening a zebrafish genomic library with a mouse Egr1 **zinc finger** probe. Southern blotting indicated the existence of single zebrafish egr1 gene and, as in higher vertebrates, the presence of related members of a larger gene family. Sequence analysis of the zebrafish egr1 coding region revealed a high level of homology to the mouse, rat, and human egr1 genes with the notable exception of a polymorphic, triplet nucleotide repeat sequence in the region coding for the amino terminus of the Egr1 protein. The predicted DNA-binding, **zinc finger** domain protein sequence was strictly conserved. The 5' region of the zebrafish egr1 gene contained a variety of transcription factor binding sites, also present in the mouse gene, for serum response factor, CREB, and c-ets. The zebrafish egr1 transcript was approximately 3.4 kb in size and was expressed in adult zebrafish brain and muscle RNA, a pattern of expression similar to that observed in mice. The potential for zebrafish egr1 to function as a transcriptional regulator was tested by constructing an expression vector containing zebrafish egr1 coding sequences under the control of a cytomegalovirus promoter. This construct was found to activate transcription of a reporter plasmid bearing multiple Egr1 binding sites when transiently cotransfected into mouse 3T3 cells. Our results indicate that the structure, regulation, and function of the Egr1 gene have been highly conserved during vertebrate evolution and suggest an important role for this gene in growth and development.
ACCESSION NUMBER: 95000298 MEDLINE
DOCUMENT NUMBER: 95000298 PubMed ID: 7917016
TITLE: The zebrafish egr1 gene encodes a highly conserved, **zinc-finger** transcriptional regulator.
AUTHOR: Drummond I A; Rohwer-Nutter P; Sukhatme V P
CORPORATE SOURCE: Harvard Medical School, Boston, MA.
CONTRACT NUMBER: CA40046 (NCI)
SOURCE: DNA AND CELL BIOLOGY, (1994 Sep) 13 (9) 953-61.
Journal code: 9004522. ISSN: 1044-5498.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U12895
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222

Entered Medline: 19941115

L5 ANSWER 6 OF 64 MEDLINE
TI **Zinc finger**-DNA recognition: analysis of base specificity by site-directed mutagenesis.
AB Zinc fingers of the **Cys2/His2 class** are conserved 28-30 amino acid motifs that constitute an important and widespread family of eukaryotic DNA-binding domains. It is therefore of great interest to understand the rules that govern specific recognition of DNA by zinc fingers. The DNA-binding domain of the transcription factor Krox-20 consists of three zinc fingers, each of them making its primary contacts with a three-base pair subsite. We have performed a data base-guided site-directed mutagenesis analysis of Krox-20: nine derivatives were generated, in which one to three amino acid changes had been introduced within finger 2, at positions which were likely to affect the specificity of DNA recognition. The affinities of the different proteins for a panel of potential DNA binding sites were estimated by gel retardation assay. Six of the derivatives bound specific targets with affinities comparable to that of wild type Krox-20 for its consensus binding site. However, the specificity of recognition was dramatically modified at the expected bases, in a manner that could be explained by examining the newly introduced amino acids within the context of the overall finger/triplet interaction. These data provide new insights into the details of **zinc finger**-DNA interactions and, combined with the modular nature of zinc fingers, illustrate both the potential and the difficulties of utilising these motifs for designing DNA-binding proteins with novel specificities.

ACCESSION NUMBER: 92375717 MEDLINE
DOCUMENT NUMBER: 92375717 PubMed ID: 1508708
TITLE: **Zinc finger**-DNA recognition: analysis of base specificity by site-directed mutagenesis.
AUTHOR: Nardelli J; Gibson T; Charnay P
CORPORATE SOURCE: Laboratoire de Genetique Moleculaire, CNRS D 1302, Ecole Normale Superieure, Paris, France.
SOURCE: NUCLEIC ACIDS RESEARCH, (1992 Aug 25) 20 (16) 4137-44. Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19921009
Last Updated on STN: 19921009
Entered Medline: 19920923

L5 ANSWER 7 OF 64 MEDLINE
TI Molecular cloning, sequencing, and mapping of EGR2, a human early growth response gene encoding a protein with "zinc-binding finger" structure.
AB Early growth response gene-1 (Egr-1) is a mouse gene displaying fos-like induction kinetics in diverse cell types following mitogenic stimulation. Egr-1 encodes a protein with "zinc-binding finger" structure. Zinc fingers are a protein structural motif that serve as DNA-binding domains in several transcriptional regulatory proteins. Using low-stringency hybridization with an Egr-1 cDNA probe, we identified a distinct human cDNA (designated EGR2 for early growth response gene-2), which is coregulated with EGR1 by fibroblast and lymphocyte mitogens; however, several stimuli that induce Egr-1 mRNA in PC12 (rat pheochromocytoma) cells do not induce Egr-2 mRNA. The cDNA sequence predicts a protein of 406 amino acids, including three tandem zinc fingers of the **Cys2-His2 class**. Strikingly, the deduced amino acid sequences of human EGR2 and mouse Egr-1 are 92% identical in the **zinc finger** region but show no similarity elsewhere. EGR2 maps to human chromosome 10 at bands q21-22. Structure-function analysis of EGR2 and EGR1 proteins should provide insight into the

mechanisms linking signal transduction and transcriptional regulation of gene expression.

ACCESSION NUMBER: 89017158 MEDLINE
DOCUMENT NUMBER: 89017158 PubMed ID: 3140236
TITLE: Molecular cloning, sequencing, and mapping of EGR2, a human early growth response gene encoding a protein with "zinc-binding finger" structure.
COMMENT: Erratum in: Proc Natl Acad Sci U S A 1989 Jan;86(2):515
AUTHOR: Joseph L J; Le Beau M M; Jamieson G A Jr; Acharya S; Shows T B; Rowley J D; Sukhatme V P
CORPORATE SOURCE: Department of Medicine, Howard Hughes Medical Institute, Chicago, IL.
CONTRACT NUMBER: CA42557 (NCI)
GM20454 (NIGMS)
GM28359 (NIGMS)
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L5 ANSWER 8 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Expression of metal response element transcription factor-1 (MTF1) via retroviral transduction normalizes metallothionein gene expression and protects cells against heavy metal toxicity.
AB MTF1 is a transcription factor that belongs to the **Cys2-His2 class** of **zinc-finger** transcription factors and is best known for its robust transcriptional regulation of vertebrate MT genes. It is, however, speculated to play a generalized role in regulating genes involved in protection against heavy metals and oxidative stress. MTF1 DNA binding is regulated by changes in the intracellular Zn+2 concentration. Molecular dissection of MTF1 has been hindered by its high constitutive trans-activity upon transient transfection. In developing a system to avoid this problem, we have employed a high efficiency retroviral transduction to reintroduce MTF1 into mouse MTF1 null cells (dk07). Murine dko7 cells exhibit no Mt expression upon Zn+2 or Cd+2 treatment, but, upon infection with a retrovirus expressing MTF1, both metals induce Mt in a dose-dependent manner. Furthermore, MTF1-retrovirally-transduced dk07 (MTF1-dk07) cells are protected against both Zn+2 and Cd+2 toxicity. Electrophoretic mobility shift assays demonstrated that MTF1-dk07 cells possess levels of inducible MTF1 binding activity, similar to the widely studied Hepa-1c1c7 cells, and MTF1 binding can be modulated over a 20-fold range by varying the concentration of Zn+2 present in the culture medium. These data suggest that the use of a retrovirus to express MTF1 in cultured cells results in basal and inducible MTF1-mediated responses phenotypically similar to wild-type cells. The system may therefore be valuable in the further dissection of functional domains of MTF1, as well as providing cell lines to study the molecular targets of this transcription factor.
ACCESSION NUMBER: 2002:233346 BIOSIS
DOCUMENT NUMBER: PREV200200233346
TITLE: Expression of metal response element transcription factor-1 (MTF1) via retroviral transduction normalizes metallothionein gene expression and protects cells against heavy metal toxicity.
AUTHOR(S): Solis, W. A. (1); Childs, N. L. (1); Nebert, D. W. (1);

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SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 731. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
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LANGUAGE: English

L5 ANSWER 9 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Retrovirally expressed metal response element-binding transcription factor-1 normalizes metallothionein-1 gene expression and protects cells against zinc, but not cadmium, toxicity.
AB Metal response element (MRE) transcription factor-1 (MTF1), a member of the **Cys2-His2 class** of **zinc-finger** transcription factors, is best known for its robust transcriptional regulation of mammalian metallothionein (MT) genes. MTF1 is also believed to play a generalized role in regulating genes involved in protection against heavy metals and oxidative stress. MTF1 binding to MRE motifs is regulated by changes in intracellular zinc (Zn2+) concentration. Molecular dissection of MTF1 has been hindered by its high constitutive trans-activity following transient transfection and the failure of these systems to examine genes packaged in native chromatin. In developing a system to avoid these problems, we employed a high-efficiency retroviral transduction system to reintroduce MTF1 into mouse Mtf1(-/-) knockout cells (dko7). Electrophoretic mobility shift assays demonstrated that MTF1 retrovirally transduced dko7 cells (MTF1dko7) possess levels of inducible MTF1-MRE binding activity similar to that seen in mouse hepatoma Hepa-1 cells, and MTF1 binding could be modulated over a 20-fold range by varying the concentration of Zn2+ present in the culture medium. The dko7 cells exhibited no change in Mt1 gene expression upon Zn2+ or cadmium (Cd2+) treatment; in contrast, in MTF1dko7 cells, Zn2+ or Cd2+ induced MT1 mRNA accumulation in a dose-dependent manner. Interestingly, MTF1dko7 cells showed resistance to Zn2+ toxicity, but negligible resistance to Cd2+. Concomitantly, MT1 protein levels in MTF1dko7 cells were inducible to the same degree as that in Hepa-1 cells when treated with Zn2+, but not with Cd2+. Together, our studies suggest that MTF1-mediated regulation of gene expression is sufficient to protect cells against Zn2+ toxicity and may be necessary but not sufficient to protect cells against Cd2+ toxicity.
ACCESSION NUMBER: 2002:174793 BIOSIS
DOCUMENT NUMBER: PREV200200174793
TITLE: Retrovirally expressed metal response element-binding transcription factor-1 normalizes metallothionein-1 gene expression and protects cells against zinc, but not cadmium, toxicity.
AUTHOR(S): Solis, Willy A.; Childs, Nicole L.; Weedon, Michael N.; He, Lei; Nebert, Daniel W.; Dalton, Timothy P. (1)
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SOURCE: Toxicology and Applied Pharmacology, (January 15, 2002) Vol. 178, No. 2, pp. 93-101. http://www.academicpress.com/tap. print.
ISSN: 0041-008X.
DOCUMENT TYPE: Article
LANGUAGE: English

L5 ANSWER 10 OF 64 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI High-resolution structures of variant Zif268-DNA complexes: Implications for understanding **zinc finger**-DNA recognition.

AB Background: Zinc fingers of the **Cys2-His2 class** comprise one of the largest families of eukaryotic DNA-binding motifs and recognize a diverse set of DNA sequences. These proteins have a relatively simple modular structure and key base contacts are typically made by a few residues from each finger. These features make the **zinc finger** motif an attractive system for designing novel DNA-binding proteins and for exploring fundamental principles of protein-DNA recognition. Results: Here we report the X-ray crystal structures of **zinc finger**-DNA complexes involving three variants of Zif268, with multiple changes in the recognition helix of finger one. We describe the structure of each of these three-finger peptides bound to its corresponding target site. To help elucidate the differential basis for site-specific recognition, the structures of four other complexes containing various combinations of these peptides with alternative binding sites have also been determined. Conclusions: The protein-DNA contacts observed in these complexes reveal the basis for the specificity demonstrated by these Zif268 variants. Many, but not all, of the contacts can be rationalized in terms of a recognition code, but the predictive value of such a code is limited. The structures illustrate how modest changes in the docking arrangement accommodate the new sidechain-base and sidechain-phosphate interactions. Such adaptations help explain the versatility of naturally occurring **zinc finger** proteins and their utility in design.

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DOCUMENT NUMBER: PREV199800302648
TITLE: High-resolution structures of variant Zif268-DNA complexes: Implications for understanding **zinc finger**-DNA recognition.
AUTHOR(S): Elrod-Erickson, Monicia; Benson, Timothy E.; Pabo, Carol O. (1)
CORPORATE SOURCE: (1) Dep. Biol., Massachusetts Inst. Technol., Cambridge, MA 02139 USA
SOURCE: Structure (London), (April 15, 1998) Vol. 6, No. 4, pp. 451-464.
ISSN: 0969-2126.
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